Supporting Information: Salt-Induced Liquid–Liquid Phase Separation: Combined Experimental and Theoretical Investigation of Water–Acetonitrile–Salt Mixtures

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Experimental Methods

Chemicals

Deionized and doubly distilled water (Water, Sigma–Aldrich, Deionized) and acetonitrile (Acetonitrile, Sigma–Aldrich, HPLC, gradient grade, $\geq 99.9\%$) were used in the experiments. The salts were dried in a vacuum oven (80°C, 133Pa) for 4 hours prior to use. We studied the following salts: lithium chloride (LiCl, Vetec, reagent grade), sodium chloride (NaCl, Sigma–Aldrich, ReagentPlus, 99%), potassium chloride (KCl, Sigma–Aldrich, anhydrous, ReagentPlus, 99%), cesium chloride (CsCl, Aladdin, 99%, AR), potassium fluoride (KF, Aladdin, 99.5%, GR), sodium bromide (NaBr, Sigma–Aldrich, anhydrous, ReagentPlus, 99%), potassium bromide (KBr, Sigma–Aldrich, anhydrous, ReagentPlus, 99%), lithium sulfate (Li_2SO_4, Aladdin, 98.5%, anhydrous, titration), sodium sulphate (Na_2SO_4, Vetec, 99.0%, reagent grade), and magnesium sulfate ($MgSO_4$, Sigma–Aldrch, 99.5%, anhydrous).

Measurements

The samples were kept in Thermo HAAKE SC150-A5B circulating water bath (Newington, U. S. A.) with a digital temperature-control unit to maintain the required temperature (25°C) within ±0.1°C and the room temperature was also kept at 25°C by air conditioner.

Cloud point

Salts were added to the solvents with fixed water–acetonitrile ratio (9.5:0.5, 9:1, 8.5:1.5, 8:2, 7.5:2.5, 7:3, 6.5:3.5, 6:4, 5:5, 4:6, 3:7, 2:8, and 1:9; V/V) until cloud points appeared.[S1–S5] The mass of water, acetonitrile, and salt were determined by Sartorius (BT 125D, Beijing, China) with an accuracy of ±0.00001g. We have measured the cloud point of ten salts (LiCl, NaCl, KCl, CsCl, KF, NaBr, KBr, Na_2SO_4, Li_2SO_4, and $MgSO_4$) in the water–acetonitrile solvents with an accuracy of ±0.01 g.

Component analysis of coexistence phases

For a given salt, a fixed mass of salt was added to a water–acetonitrile solvent (volume

ratio of water to acetonitrile is 1:1), and the mixture was held for at least 8 hours in the circulating water bath at 25°C. We do the same operations and by changing the mass of the salt (ranging from cloud point to saturation of the system). When the WAS system reached phase equilibrium, the acetonitrile-rich phase and water-rich phase were taken out by syringing and their volume and mass were measured respectively. The content of acetonitrile and water were determined by gas chromatography (GC, Themo, Trace, GC, Ultra) in the coexisting phases (acetonitrile-rich and water-rich phases). For the acetonitrile-rich phase, the content of salts was determined by inductive coupled plasma optical emission spectrometer (ICP-OES, Themo, iCAP 6300 ICP-OES). As for the water-rich phase, the content of the following six salts (NaCl, KCl, CsCl, NaBr, KBr, and Na_2SO_4) were determined by mass. More specifically, the solutions were first kept in the oven (80°C) at ambient pressure and then were dried in a vacuum oven (80°C, 133Pa) until the solvents were completely evaporated. The contents of the remaining salts (LiCl, Li_2SO_4 and $MgSO_4$) were also determined by ICP-OES. The mass fraction errors of GC and ICP-OES are -3.39% to 3.63% and -2.90% to 4.09%, respectively.

Solubility of salts

For a given salt, excessive salt was added to water–acetonitrile solvents (volume ratios of water to acetonitrile were 7:3, 6:4, 5:5, 4:6, and 3:7), and the mixtures were dissolved by ultrasound and held for at least 8 hours in the circulating water bath at 25°C. The liquid was taken out by the syringe. The remaining salt (for NaCl, KCl, CsCl, NaBr, KBr, and Na_2SO_4) precipitated at the bottom was filtered by filter paper and then dried completely. The mass of the dissolved salt is calculated as, the total input of salt minus the amount of the precipitated salt. For the solubility of LiCl, Li_2SO_4, and $MgSO_4$, we refer to the work of Meng et al.[S6,S7] The specific procedures are as follows: adding doubly distilled water to the test tube after removing the liquid, dissolving the precipitated salt with crystalloid water, and then transferring them to volumetric flask. Finally, the mass of salts in the volumetric flask (the remaining salt without crystalloid water) was determined by ICP-OES. The mass

of the dissolved salt is calculated as follows, the total input of salt minus the amount of the rest salt without crystalloid water.

Thermodynamics of the Water–Acetonitrile–Salt System

Alternative derivation of the hydration free energy

In this section, we provide an alternative derivation of the hydration free energy without using the combinatorial argument. We consider an incompressible mixture of water, acetonitrile and salt ions. For simplicity, we assume these entities have the same volume v. The ions can be either free or hydrated with hydration numbers p and m for the cations and anions, respectively. The water molecules can either hydrate the ions or be free. We further assume that the system volume V is not affected by the composition or hydration state and is given by an incompressibility constraint $V = (n_\mathrm{w} + n_\mathrm{a} + n_+ + n_-)\, v$. Thus, we only need to consider the ideal part of the Helmholtz free energy, since the excess part will be independent of composition and hence does not contribute to the free energy of mixing. For this consideration, we ignore the electrostatic interactions and the Born energy. Treating the free and hydrated ions as different species, the ideal part of the Helmholtz free energy is:

$$\begin{aligned}
\frac{F^\mathrm{mix}}{RT} &= \sum_i n_i \left(\frac{\mu_i^*}{RT} + \ln \frac{n_i v}{V} - 1 \right) \\
&= n_\mathrm{w,f} \left(\frac{\mu_\mathrm{w}^*}{RT} + \ln \frac{n_\mathrm{w,f} v}{V} - 1 \right) + n_\mathrm{a} \left(\frac{\mu_\mathrm{a}^*}{RT} + \ln \frac{n_\mathrm{a} v}{V} - 1 \right) \\
&+ n_\mathrm{+,f} \left(\frac{\mu_\mathrm{+,f}^*}{RT} + \ln \frac{n_\mathrm{+,f} v}{V} - 1 \right) + n_\mathrm{-,f} \left(\frac{\mu_\mathrm{-,f}^*}{RT} + \ln \frac{n_\mathrm{-,f} v}{V} - 1 \right) \\
&+ n_\mathrm{+,h} \left(\frac{\mu_\mathrm{+,h}^*}{RT} + \ln \frac{n_\mathrm{+,h} v}{V} - 1 \right) + n_\mathrm{-,h} \left(\frac{\mu_\mathrm{-,h}^*}{RT} + \ln \frac{n_\mathrm{-,h} v}{V} - 1 \right)
\end{aligned} \tag{S1}$$

n_i is the mole of species i, R is the universal gas constant, and T is the temperature. μ_w^*, μ_a^*, $\mu_\mathrm{+,f}^*$, $\mu_\mathrm{-,f}^*$, $\mu_\mathrm{+,h}^*$, and $\mu_\mathrm{-,h}^*$ are the reference chemical potential of water, acetonitrile, free cations, free anions, hydrated cations, and hydrated anions, respectively. The subscript "h"

is for hydrated ions, and "f" is for free ions or free water molecules. The number of free water molecules and ions are $n_{\mathrm{w,f}} = n_{\mathrm{w}} - pn_{+,\mathrm{h}} - mn_{-,\mathrm{h}}$ and $n_{\pm,\mathrm{f}} = (n_{\pm} - n_{\pm,\mathrm{h}})$. The hydrating water molecules on each ion are indistinguishable, so they contribute $n_{+,\mathrm{h}} \ln(p!)$ and $n_{-,\mathrm{h}} \ln(m!)$ respectively to $\mu^*_{+,\mathrm{h}}$ and $\mu^*_{-,\mathrm{h}}$.

Minimizing the free energy with respect to $n_{+,\mathrm{h}}$ and $n_{-,\mathrm{h}}$, subject to fixed total number of ions $n_{+,\mathrm{f}} + n_{+,\mathrm{h}} = n_{+,\mathrm{f}}$ and $n_{-,\mathrm{f}} + n_{-,\mathrm{h}} = n_{-,\mathrm{f}}$, we have

$$\ln \frac{n_{+,\mathrm{h}} v}{V} - \ln \frac{(n_+ - n_{+,\mathrm{h}})\, v}{V} - p \ln \frac{(n_{\mathrm{w}} - pn_{+,\mathrm{h}} - mn_{-,\mathrm{h}})\, v}{V} = -\left(\frac{\mu^*_{+,\mathrm{h}}}{RT} - p\frac{\mu^*_{\mathrm{w}}}{RT} - \frac{\mu^*_{+,\mathrm{f}}}{RT} \right) \quad \text{(S2)}$$

and

$$\ln \frac{n_{-,\mathrm{h}} v}{V} - \ln \frac{(n_- - n_{-,\mathrm{h}})\, v}{V} - m \ln \frac{(n_{\mathrm{w}} - pn_{+,\mathrm{h}} - mn_{-,\mathrm{h}})\, v}{V} = -\left(\frac{\mu^*_{-,\mathrm{h}}}{RT} - m\frac{\mu^*_{\mathrm{w}}}{RT} - \frac{\mu^*_{-,\mathrm{f}}}{RT} \right) \quad \text{(S3)}$$

where the right side of "=" in the parentheses is the hydration free energy.

$$f^{\mathrm{hyd}}_{+} = \mu^*_{+,\mathrm{h}} - p\mu^*_{\mathrm{w}} - \mu^*_{+,\mathrm{f}} \equiv E^{\mathrm{hyd}}_{+} + RT \ln(p!) \quad \text{(S4)}$$

and

$$f^{\mathrm{hyd}}_{-} = \mu^*_{-,\mathrm{h}} - m\mu^*_{\mathrm{w}} - \mu^*_{-,\mathrm{f}} \equiv E^{\mathrm{hyd}}_{-} + RT \ln(m!) \quad \text{(S5)}$$

We can write Eq S2 and S3 in the form of " chemical equilibrium constant":

$$\frac{(n_{+,\mathrm{h}} v/V)}{[(n_+ - n_{+,\mathrm{h}})\, v/V]\, [(n_{\mathrm{w}} - pn_{+,\mathrm{h}} - mn_{-,\mathrm{h}})\, v/V]^p} = \exp\left(-\frac{f^{\mathrm{hyd}}_{+}}{RT} \right) \quad \text{(S6)}$$

and

$$\frac{(n_{-,\mathrm{h}} v/V)}{[(n_- - n_{-,\mathrm{h}})\, v/V]\, [(n_{\mathrm{w}} - pn_{+,\mathrm{h}} - mn_{-,\mathrm{h}})\, v/V]^m} = \exp\left(-\frac{f^{\mathrm{hyd}}_{-}}{RT} \right) \quad \text{(S7)}$$

Since these hydration free energies are very large and negative (the energies given in Table 1 are at least order 100 RT; the free energy will be of comparable magnitude), the equilibrium

constant is very large. So to a very good approximation, the fraction of free ions is negligible, and we can set $n_{\pm,\mathrm{f}} = 0$ and $n_{\pm,\mathrm{h}} = n_{\pm}$. The free energy is simplified to

$$\begin{aligned}\frac{F^{\mathrm{mix}}}{RT} &= (n_{\mathrm{w}} - pn_{+} - mn_{-})\,\frac{\mu^{*}_{\mathrm{w}}}{RT} + n_{\mathrm{a}}\frac{\mu^{*}_{\mathrm{a}}}{RT} + n_{+}\frac{\mu^{*}_{+,\mathrm{h}}}{RT} + n_{-}\frac{\mu^{*}_{-,\mathrm{h}}}{RT} \\ &\quad + (n_{\mathrm{w}} - pn_{+} - mn_{-})\ln\frac{(n_{\mathrm{w}} - pn_{+} - mn_{-})\,v}{V} - (n_{\mathrm{w}} - pn_{+} - mn_{-}) + n_{\mathrm{a}}\ln\frac{n_{\mathrm{a}}v}{V} - n_{\mathrm{a}} \\ &\quad + n_{+}\ln\frac{n_{+}v}{V} - n_{+} + n_{-}\ln\frac{n_{-}v}{V} - n_{-}\end{aligned} \tag{S8}$$

Because of electroneutrality, the mole numbers of cations and anions are not independent; they are related to the mole number of salts as $n_{+} = \alpha n_{\mathrm{s}}$ and $n_{-} = \beta n_{\mathrm{s}}$. Taking the volume incompressibility constraint and electroneutrality into account, we get:

$$\begin{aligned}\frac{F^{\mathrm{mix}}}{RT} &= [n_{\mathrm{w}} - (p\alpha + m\beta)\,n_{\mathrm{s}}]\left[\frac{\mu^{*}_{\mathrm{w}}}{RT} + \ln\frac{n_{\mathrm{w}} - (p\alpha + m\beta)\,n_{\mathrm{s}}}{n_{\mathrm{w}} + n_{\mathrm{a}} + (\alpha+\beta)\,n_{\mathrm{s}}} - 1\right] \\ &\quad + n_{\mathrm{a}}\left[\frac{\mu^{*}_{\mathrm{a}}}{RT} + \ln\frac{n_{\mathrm{a}}}{n_{\mathrm{w}} + n_{\mathrm{a}} + (\alpha+\beta)\,n_{\mathrm{s}}} - 1\right] \\ &\quad + n_{\mathrm{s}}\left[\frac{\mu^{*}_{\mathrm{s,h}}}{RT} + (\alpha+\beta)\ln\frac{n_{\mathrm{s}}}{n_{\mathrm{w}} + n_{\mathrm{a}} + (\alpha+\beta)\,n_{\mathrm{s}}} - (\alpha+\beta)\right]\end{aligned} \tag{S9}$$

where $\mu^{*}_{\mathrm{s,h}} \equiv \alpha\mu^{*}_{+,\mathrm{h}} + \beta\mu^{*}_{-,\mathrm{h}} + RT\,(\alpha\ln\alpha + \beta\ln\beta)$

To isolate the hydration part of the free energy, we subtract the ideal part of mixing free ions with water and acetonitrile, which is

$$\begin{aligned}\frac{F^{\mathrm{id}}}{RT} &= n_{\mathrm{w}}\frac{\mu^{*}_{\mathrm{w}}}{RT} + n_{\mathrm{a}}\frac{\mu^{*}_{\mathrm{a}}}{RT} + \alpha n_{\mathrm{s}}\frac{\mu^{*}_{+,\mathrm{f}}}{RT} + \beta n_{\mathrm{s}}\frac{\mu^{*}_{-,\mathrm{f}}}{RT} \\ &\quad + n_{\mathrm{a}}\ln\frac{n_{\mathrm{a}}v}{V} - n_{\mathrm{a}} + \alpha n_{\mathrm{s}}\ln\frac{\alpha n_{\mathrm{s}}v}{V} - \alpha n_{\mathrm{s}} + \beta n_{\mathrm{s}}\ln\frac{\beta n_{\mathrm{s}}v}{V} - \beta n_{\mathrm{s}} \\ &\quad + n_{\mathrm{w}}\ln\frac{n_{\mathrm{w}}v}{V} - n_{\mathrm{w}}\end{aligned} \tag{S10}$$

Taking the difference between Eq S8 and Eq S10 and substituting Eqs. S4-S5, we obtain

$$\begin{aligned}\frac{F^{\mathrm{hyd}}}{RT} = n_{\mathrm{s}} &\left(\alpha\frac{E_{+}^{\mathrm{hyd}}}{RT} + \beta\frac{E_{-}^{\mathrm{hyd}}}{RT} + \alpha\ln p! + \beta\ln m!\right) \\ &+ \left[n_{\mathrm{w}} - (p\alpha + m\beta)\, n_{\mathrm{s}}\right]\ln\left[1 - (p\alpha + m\beta)\,\frac{n_{\mathrm{s}}}{n_{\mathrm{w}}}\right] \\ &- (p\alpha + m\beta)\, n_{\mathrm{s}}\ln\frac{n_{\mathrm{w}}v}{V} + (p\alpha + m\beta)\, n_{\mathrm{s}}\end{aligned} \tag{S11}$$

Substituting the volume from the incompressibility constraint, and noting that for an incompressible system, the hydration Gibbs free energy is the same as the hydration Helmholtz free energy, we recover Eq 10 in the main text.

Excess free energy for water-acetonitrile mixture

The water–acetonitrile excess free energy of mixing can be written as

$$G^{\mathrm{w/a}} = n_{\mathrm{w}}RT\ln\gamma_{\mathrm{w}}^{\mathrm{w/a}} + n_{\mathrm{a}}RT\ln\gamma_{\mathrm{a}}^{\mathrm{w/a}} \tag{S12}$$

where $\gamma_{\mathrm{w}}^{\mathrm{w/a}}$ and $\gamma_{\mathrm{a}}^{\mathrm{w/a}}$ are the activity coefficients of water and acetonitrile. We define $g^{\mathrm{w/a}} = \omega\ln\gamma_{\mathrm{w}}^{\mathrm{w/a}} + (1-\omega)\ln\gamma_{\mathrm{a}}^{\mathrm{w/a}}$, where ω is the water mole fraction in the liquid $\omega = \frac{n_{\mathrm{w}}}{n_{\mathrm{w}}+n_{\mathrm{a}}}$. For the expression of $g^{\mathrm{w/a}}$, we compared the Villamañán's model[S8] and Shealy's model[S9] in Figure S1 with French's experimental data (25°C),[S10] the former fits better. Thus, we choose Villamañán's model, which is given by

$$\begin{aligned}\frac{g^{\mathrm{w/a}}}{\omega(1-\omega)} =& \mathscr{A}\omega + \mathscr{B}(1-\omega) + [\mathscr{C}\omega + \mathscr{D}(1-\omega)]\omega(1-\omega) + [\mathscr{E}\omega + \mathscr{F}(1-\omega)][\omega(1-\omega)]^2 \\ &+ [\mathscr{G}\omega + \mathscr{H}(1-\omega)][\omega(1-\omega)]^3\end{aligned} \tag{S13}$$

The values of parameters $\mathscr{A}$ to $\mathscr{H}$ are listed in Table S1.

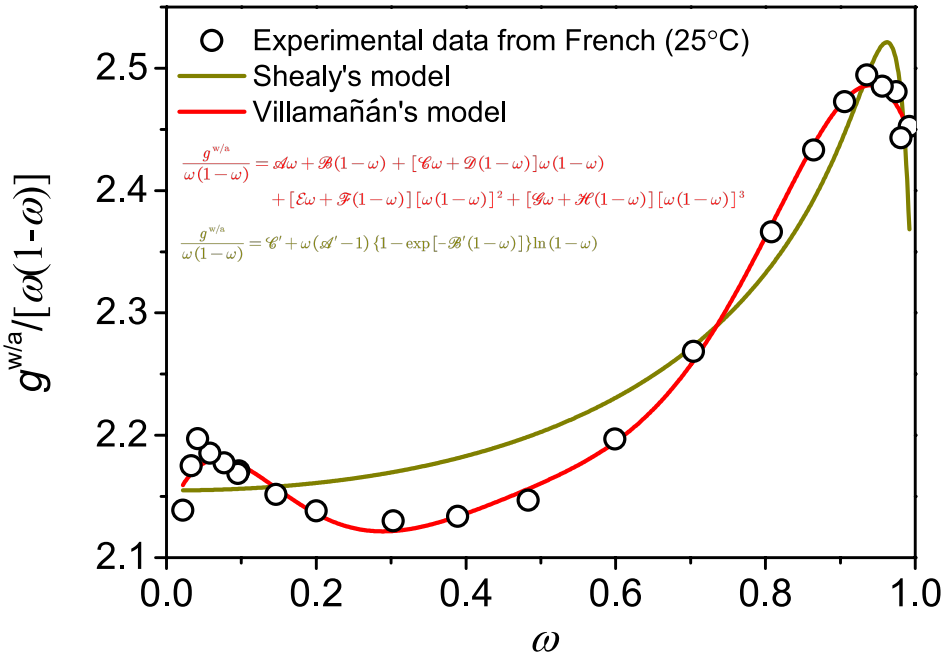

Figure S1: Experimental and fitting data for excess molar Gibbs free energy of water–acetonitrile mixture.

Table S1: Fitting Parameters in Eq (S13)

$\mathscr{A}$	$\mathscr{B}$	$\mathscr{C}$	$\mathscr{D}$	$\mathscr{E}$	$\mathscr{F}$	$\mathscr{G}$	$\mathscr{H}$
2.433	2.129	2.294	1.471	-19.157	-19.55	31.27	47.921

The final expression of $G^{\mathrm{w/a}}$ is

$$G^{\mathrm{w/a}} = (n_{\mathrm{w}} + n_{\mathrm{a}})\, RT g^{\mathrm{w/a}}(\omega) \tag{S14}$$

Electrostatic free energy from mean-spherical-approximation (MSA)

For the equal ion sizes, invoking charge neutrality, the electrostatic part of the free energy from the MSA theory[S11] ($G^{\mathrm{ele}}_{\mathrm{MSA}}$) is written as

$$G^{\mathrm{ele}}_{\mathrm{MSA}} = -RT\frac{V}{\pi}\Theta^3\left(\frac{2}{3} + \Theta a_0\right) \tag{S15}$$

The screening parameter Θ satisfies $\Theta(1 + \Theta\sigma) = \kappa/2$, where κ is the inverse Debye screening length given by Eq 12 in the main text for a single solvent. At present, a systematic modification of MSA for binary solvent with different dielectric constant for each component is not available. We thus make the ad hoc approximation by using a simple volume-fraction average of the dielectric constant of the two liquids.

Total free energy and chemical potential

With expressions of G^{id}, G^{hyd}, G^{ele}, G^{Born}, and $G^{\mathrm{w/a}}$. We have the total Gibbs free energy of the WAS system $G_{\mathrm{DH}}(n_{\mathrm{w}}, n_{\mathrm{a}}, n_{\mathrm{s}})$ and $G_{\mathrm{MSA}}(n_{\mathrm{w}}, n_{\mathrm{a}}, n_{\mathrm{s}})$ based on Debye-Hückel (DH) and

based on MSA, respectively:

$$\begin{aligned}\frac{G_{\mathrm{DH}}\left(n_{\mathrm{w}},n_{\mathrm{a}},n_{\mathrm{s}}\right)}{RT} &= n_{\mathrm{w}}\left(\frac{\mu_{\mathrm{w}}^{*}}{RT}+\ln x_{\mathrm{w}}\right)+n_{\mathrm{a}}\left(\frac{\mu_{\mathrm{a}}^{*}}{RT}+\ln x_{\mathrm{a}}\right)+n_{\mathrm{s}}\left[\frac{\mu_{\mathrm{s}}^{*}}{RT}+(\alpha+\beta)\ln x_{\mathrm{s}}\right]\\ &+ n_{\mathrm{w}}\ln\left[1-(p\alpha+m\beta)\frac{n_{\mathrm{s}}}{n_{\mathrm{w}}}\right]\\ &- (p\alpha+m\beta)n_{\mathrm{s}}\ln\frac{n_{\mathrm{w}}-(p\alpha+m\beta)n_{\mathrm{s}}}{n_{\mathrm{w}}+n_{\mathrm{a}}+(\alpha+\beta)n_{\mathrm{s}}}+(p\alpha+m\beta)n_{\mathrm{s}}\\ &- \frac{v_{\mathrm{w}}}{4\pi a_0^3}\left(n_{\mathrm{w}}+\tau n_{\mathrm{a}}\right)\left[\ln\left(1+\kappa a_0\right)-\kappa a_0+\frac{1}{2}\left(\kappa a_0\right)^2\right]\\ &+ \frac{N_{\mathrm{av}}e^2\left(\alpha z_+^2+\beta z_-^2\right)n_{\mathrm{s}}}{8\pi\epsilon_0 a_0 RT}\frac{n_{\mathrm{w}}+\tau n_{\mathrm{a}}}{n_{\mathrm{w}}\epsilon_{\mathrm{w}}+\tau n_{\mathrm{a}}\epsilon_{\mathrm{a}}}\\ &+ \left(n_{\mathrm{w}}+n_{\mathrm{a}}\right)g^{\mathrm{w/a}}(\omega)\end{aligned} \tag{S16}$$

$$\begin{aligned}\frac{G_{\mathrm{MSA}}\left(n_{\mathrm{w}},n_{\mathrm{a}},n_{\mathrm{s}}\right)}{RT} &= n_{\mathrm{w}}\left(\frac{\mu_{\mathrm{w}}^{*}}{RT}+\ln x_{\mathrm{w}}\right)+n_{\mathrm{a}}\left(\frac{\mu_{\mathrm{a}}^{*}}{RT}+\ln x_{\mathrm{a}}\right)+n_{\mathrm{s}}\left[\frac{\mu_{\mathrm{s}}^{*}}{RT}+(\alpha+\beta)\ln x_{\mathrm{s}}\right]\\ &+ n_{\mathrm{w}}\ln\left[1-(p\alpha+m\beta)\frac{n_{\mathrm{s}}}{n_{\mathrm{w}}}\right]\\ &- (p\alpha+m\beta)n_{\mathrm{s}}\ln\frac{n_{\mathrm{w}}-(p\alpha+m\beta)n_{\mathrm{s}}}{n_{\mathrm{w}}+n_{\mathrm{a}}+(\alpha+\beta)n_{\mathrm{s}}}+(p\alpha+m\beta)n_{\mathrm{s}}\\ &- \frac{v_{\mathrm{w}}\left(n_{\mathrm{w}}+\tau n_{\mathrm{a}}\right)}{16a_0^3\pi}\left(\frac{1}{3}+\sqrt{2a_0\kappa+1}\right)\left(-1+\sqrt{2a_0\kappa+1}\right)^3\\ &+ \frac{N_{\mathrm{av}}e^2\left(\alpha z_+^2+\beta z_-^2\right)n_{\mathrm{s}}}{8\pi\epsilon_0 a_0 RT}\frac{n_{\mathrm{w}}+\tau n_{\mathrm{a}}}{n_{\mathrm{w}}\epsilon_{\mathrm{w}}+\tau n_{\mathrm{a}}\epsilon_{\mathrm{a}}}\\ &+ \left(n_{\mathrm{w}}+n_{\mathrm{a}}\right)g^{\mathrm{w/a}}(\omega)\end{aligned} \tag{S17}$$

where we have redefined the reference chemical potential of the salt to absorb the hydration energy:

$$\frac{\mu_{\mathrm{s}}^{*}}{RT}=\frac{\mu_{\mathrm{s,f}}^{*}}{RT}+\alpha\frac{E_{+}^{\mathrm{hyd}}}{RT}+\beta\frac{E_{-}^{\mathrm{hyd}}}{RT}+\alpha\ln p!+\beta\ln m! \tag{S18}$$

and τ stands for the volume ratio of acetonitrile to water $\tau = v_{\mathrm{a}}/v_{\mathrm{w}}$ in the electrostatic part of the free energy. The chemical potential of the different species are then obtained from $\mu_{\mathrm{w}} = \frac{\partial G}{\partial n_{\mathrm{w}}}$, $\mu_{\mathrm{a}} = \frac{\partial G}{\partial n_{\mathrm{a}}}$ and $\mu_{\mathrm{s}} = \frac{\partial G}{\partial n_{\mathrm{s}}}$. For convenience, we represent the composition using the

mole fraction of water in the binary liquid $\omega = n_{\mathrm{w}}/(n_{\mathrm{w}} + n_{\mathrm{a}})$, and the molar ratio of salt to water $r = n_{\mathrm{s}}/n_{\mathrm{w}}$.

For the chemical potentials of water, acetonitrile and salt we write them in the following form

$$\mu_i = \mu_i^{\mathrm{id}} + \mu_i^{\mathrm{hyd}} + \mu_i^{\mathrm{ele}} + \mu_i^{\mathrm{Born}} + \mu_i^{\mathrm{w/a}} \tag{S19}$$

where i=w, a, or s. μ_i^{id}, μ_i^{hyd}, μ_i^{ele}, μ_i^{Born}, and $\mu_i^{\mathrm{w/a}}$ refer to the chemical potential contribution from ideal mixing, hydration effect, electrostatic interactrions, Born energy, and excess free energy of the water–acetonitrile mixture. $\mu_i^{\mathrm{ele(DH)}}$ and $\mu_i^{\mathrm{ele(MSA)}}$ are the electrostatic interaction contributions calculated by DH and MSA.

For the chemical potential of water, we have

$$\frac{\mu_{\mathrm{w}}^{\mathrm{id}}}{RT} = \frac{\mu_{\mathrm{w}}^{*}}{RT} + \ln \frac{\omega}{1 + (\alpha + \beta)\,\omega r} \tag{S20}$$

$$\frac{\mu_{\mathrm{w}}^{\mathrm{hyd}}}{RT} = \ln\left[1 - (p\alpha + m\beta)\, r\right] + \frac{(p\alpha + m\beta)\,\omega r}{1 + (\alpha + \beta)\,\omega r} \tag{S21}$$

$$\frac{\mu_{\mathrm{w}}^{\mathrm{ele(DH)}}}{RT} = -\frac{v_{\mathrm{w}}}{4\pi a_0^3}\left[\ln\left(1 + \kappa a_0\right) - \kappa a_0 + \frac{1}{2}\left(\kappa a_0\right)^2\right] + \frac{v_{\mathrm{w}}}{8\pi a_0^3}\frac{\left(\kappa a_0\right)^3}{1 + \kappa a_0}\frac{\left[\omega + \tau\left(1 - \omega\right)\right]\epsilon_{\mathrm{w}}}{\omega\epsilon_{\mathrm{w}} + \tau\left(1 - \omega\right)\epsilon_{\mathrm{a}}} \tag{S22}$$

$$\frac{\mu_{\mathrm{w}}^{\mathrm{ele(MSA)}}}{RT} = \left[\frac{v_{\mathrm{w}}\left(-1 + \sqrt{2a_0\kappa + 1}\right)}{24\pi a_0^3} - \frac{v_{\mathrm{w}}\kappa}{8\pi a_0^2}\frac{\tau\left(1 - \omega\right)\left(\epsilon_{\mathrm{a}} - \epsilon_{\mathrm{w}}\right)}{\omega\epsilon_{\mathrm{w}} + \tau\left(1 - \omega\right)\epsilon_{\mathrm{a}}}\right]\left(-1 + \sqrt{2a_0\kappa + 1}\right)^2 \tag{S23}$$

$$\frac{\mu_{\mathrm{w}}^{\mathrm{Born}}}{RT} = \frac{N_{\mathrm{av}}e^2\left(\alpha z_+^2 + \beta z_-^2\right)}{8\pi\epsilon_0 a_0 RT}\frac{\tau\omega r\left(1 - \omega\right)\left(\epsilon_{\mathrm{a}} - \epsilon_{\mathrm{w}}\right)}{\left[\omega\epsilon_{\mathrm{w}} + \tau\left(1 - \omega\right)\epsilon_{\mathrm{a}}\right]^2} \tag{S24}$$

$$\frac{\mu_{\mathrm{w}}^{\mathrm{w/a}}}{RT} = g^{\mathrm{w/a}} + \left(1 - \omega\right)\frac{\mathrm{d}g^{\mathrm{w/a}}}{\mathrm{d}\omega} \tag{S25}$$

For the chemical potential of acetonitrile, we have

$$\frac{\mu_{\mathrm{a}}^{\mathrm{id}}}{RT} = \frac{\mu_{\mathrm{a}}^{*}}{RT} + \ln \frac{1 - \omega}{1 + (\alpha + \beta)\,\omega r} \tag{S26}$$

$$\frac{\mu_{\mathrm{a}}^{\mathrm{hyd}}}{RT} = \frac{(p\alpha + m\beta)\,\omega r}{1 + (\alpha + \beta)\,\omega r} \tag{S27}$$

$$\frac{\mu_{\mathrm{a}}^{\mathrm{ele(DH)}}}{RT}=-\frac{\tau v_{\mathrm{w}}}{4\pi a_0^3}\left[\ln\left(1+\kappa a_0\right)-\kappa a_0+\frac{1}{2}\left(\kappa a_0\right)^2\right]+\frac{v_{\mathrm{w}}}{8\pi a_0^3}\frac{\left(\kappa a_0\right)^3}{1+\kappa a_0}\frac{\left[\omega+\tau\left(1-\omega\right)\right]\tau\epsilon_{\mathrm{a}}}{\omega\epsilon_{\mathrm{w}}+\tau\left(1-\omega\right)\epsilon_{\mathrm{a}}} \tag{S28}$$

$$\frac{\mu_{\mathrm{a}}^{\mathrm{ele(MSA)}}}{RT}=\left[\frac{\tau v_{\mathrm{w}}\left(-1+\sqrt{2a_0\kappa+1}\right)}{24\pi a_0^3}+\frac{v_{\mathrm{w}}\kappa}{8\pi a_0^2}\frac{\tau\omega\left(\epsilon_{\mathrm{a}}-\epsilon_{\mathrm{w}}\right)}{\omega\epsilon_{\mathrm{w}}+\tau\left(1-\omega\right)\epsilon_{\mathrm{a}}}\right]\left(-1+\sqrt{2a_0\kappa+1}\right)^2 \tag{S29}$$

$$\frac{\mu_{\mathrm{a}}^{\mathrm{Born}}}{RT}=\frac{N_{\mathrm{av}}e^2\left(\alpha z_+^2+\beta z_-^2\right)}{8\pi\epsilon_0 a_0 RT}\frac{\tau\omega^2 r\left(\epsilon_{\mathrm{w}}-\epsilon_{\mathrm{a}}\right)}{\left[\omega\epsilon_{\mathrm{w}}+\tau\left(1-\omega\right)\epsilon_{\mathrm{a}}\right]^2} \tag{S30}$$

$$\frac{\mu_{\mathrm{a}}^{\mathrm{w/a}}}{RT}=g^{\mathrm{w/a}}-\omega\frac{\mathrm{d}g^{\mathrm{w/a}}}{\mathrm{d}\omega} \tag{S31}$$

For the chemical potential of salt, we have

$$\frac{\mu_{\mathrm{s}}^{\mathrm{id}}}{RT}=\frac{\mu_{\mathrm{s}}^{*}}{RT}+\left(\alpha+\beta\right)\ln\frac{\omega r}{1+\left(\alpha+\beta\right)\omega r} \tag{S32}$$

$$\frac{\mu_{\mathrm{s}}^{\mathrm{hyd}}}{RT}=-\left(p\alpha+m\beta\right)\ln\frac{\omega-\left(p\alpha+m\beta\right)\omega r}{1+\left(\alpha+\beta\right)\omega r}+\frac{\left(p\alpha+m\beta\right)\left(\alpha+\beta\right)\omega r}{1+\left(\alpha+\beta\right)\omega r} \tag{S33}$$

$$\frac{\mu_{\mathrm{s}}^{\mathrm{ele(DH)}}}{RT}=-\frac{v_{\mathrm{w}}}{8\pi a_0^3}\frac{\left(\kappa a_0\right)^3}{1+\kappa a_0}\frac{\omega+\tau\left(1-\omega\right)}{\omega r} \tag{S34}$$

$$\frac{\mu_{\mathrm{s}}^{\mathrm{ele(MSA)}}}{RT}=-\frac{v_{\mathrm{w}}\kappa}{8\pi a_0^2}\frac{\omega+\tau\left(1-\omega\right)}{\omega r}\left(-1+\sqrt{2a_0\kappa+1}\right)^2 \tag{S35}$$

$$\frac{\mu_{\mathrm{s}}^{\mathrm{Born}}}{RT}=\frac{N_{\mathrm{av}}e^2\left(\alpha z_+^2+\beta z_-^2\right)}{8\pi\epsilon_0 a_0 RT}\frac{\omega+\tau\left(1-\omega\right)}{\omega\epsilon_{\mathrm{w}}+\tau\left(1-\omega\right)\epsilon_{\mathrm{a}}} \tag{S36}$$

The inverse Debye screening length κ written in terms of ω and r is

$$\kappa^2=\frac{e^2}{\epsilon_0 k_{\mathrm{B}}T}\frac{\alpha z_+^2+\beta z_-^2}{v_{\mathrm{w}}}\frac{\omega r}{\omega\epsilon_{\mathrm{w}}+\tau\left(1-\omega\right)\epsilon_{\mathrm{a}}} \tag{S37}$$

Critical point

The critical point is calculated from a semi-open system thermodynamic potential. We consider one composition variable $c=\frac{n_{\mathrm{s}}}{n_{\mathrm{w}}+n_{\mathrm{a}}}$ as in a canonical ensemble and obtain its equilibrium value in terms of the other variable ω. We consider a semi-open system with the

following free energy normalized to $(n_{\mathrm{w}} + n_{\mathrm{a}})$.

$$\varphi = g\left(\omega, c\right) - c\mu_{\mathrm{s}} \tag{S38}$$

where $g\left(\omega, c\right)$ is the Gibbs free energy normalized to $(n_{\mathrm{w}} + n_{\mathrm{a}})$, it is just the right hand side of Eq (**??**). μ_{s} is variable to c. Minimizing this free energy with respect to c, we have

$$g_c^{'} - \mu_{\mathrm{s}} = 0 \tag{S39}$$

We perform the derivative on both sides of the equation

$$g_{c\omega}^{''} + g_{cc}^{''}\frac{\mathrm{d}c}{\mathrm{d}\omega} = 0 \tag{S40}$$

$$\frac{\mathrm{d}c}{\mathrm{d}\omega} = -\frac{g_{c\omega}^{''}}{g_{cc}^{''}} \tag{S41}$$

For the first derivate of the grand free energy with respect to ω, we have

$$\frac{\mathrm{d}\varphi}{\mathrm{d}\omega} = g_{\omega}^{'} + g_c^{'}\frac{\mathrm{d}c}{\mathrm{d}\omega} - \mu_{\mathrm{s}}\frac{\mathrm{d}c}{\mathrm{d}\omega} \tag{S42}$$

Substituting Eq (S39) into Eq (S42)

$$\frac{\mathrm{d}\varphi}{\mathrm{d}\omega} = g_{\omega}^{'} \tag{S43}$$

The second derivative is

$$\frac{\mathrm{d}^2\varphi}{\mathrm{d}\omega^2} = g_{\omega\omega}^{''} + g_{\omega c}^{''}\frac{\mathrm{d}c}{\mathrm{d}\omega} \tag{S44}$$

The third derivative is

$$\frac{\mathrm{d}^3\varphi}{\mathrm{d}\omega^3} = g_{\omega\omega\omega}^{'''} + 3g_{\omega\omega c}^{'''}\frac{\mathrm{d}c}{\mathrm{d}\omega} + 3g_{\omega cc}^{'''}\left(\frac{\mathrm{d}c}{\mathrm{d}\omega}\right)^2 + g_{ccc}^{'''}\left(\frac{\mathrm{d}c}{\mathrm{d}\omega}\right)^3 \tag{S45}$$

The critical point is calculated by $\frac{\mathrm{d}^2\varphi}{\mathrm{d}\omega^2} = \frac{\mathrm{d}^3\varphi}{\mathrm{d}\omega^3} = 0$, and we use the relation $r = \frac{c}{\omega}$ to calculate r.

Comparison of theoretical phase diagrams calculated by DH vs. MSA

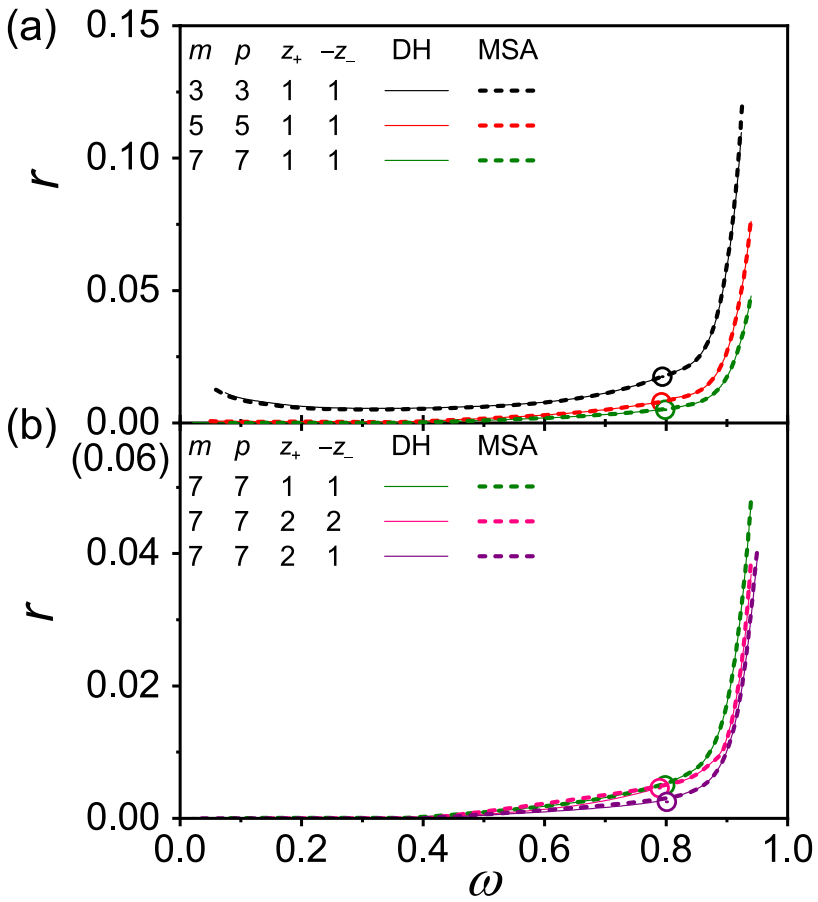

Figure S2: Comparison of theoretical phase diagrams of the WAS system calculated by the Debye-Hückel theory (DH) and the mean spherical approximation theory (MSA) for Debye radius $a_0 = 4.56$.

Effects of ion radius on the phase diagrams

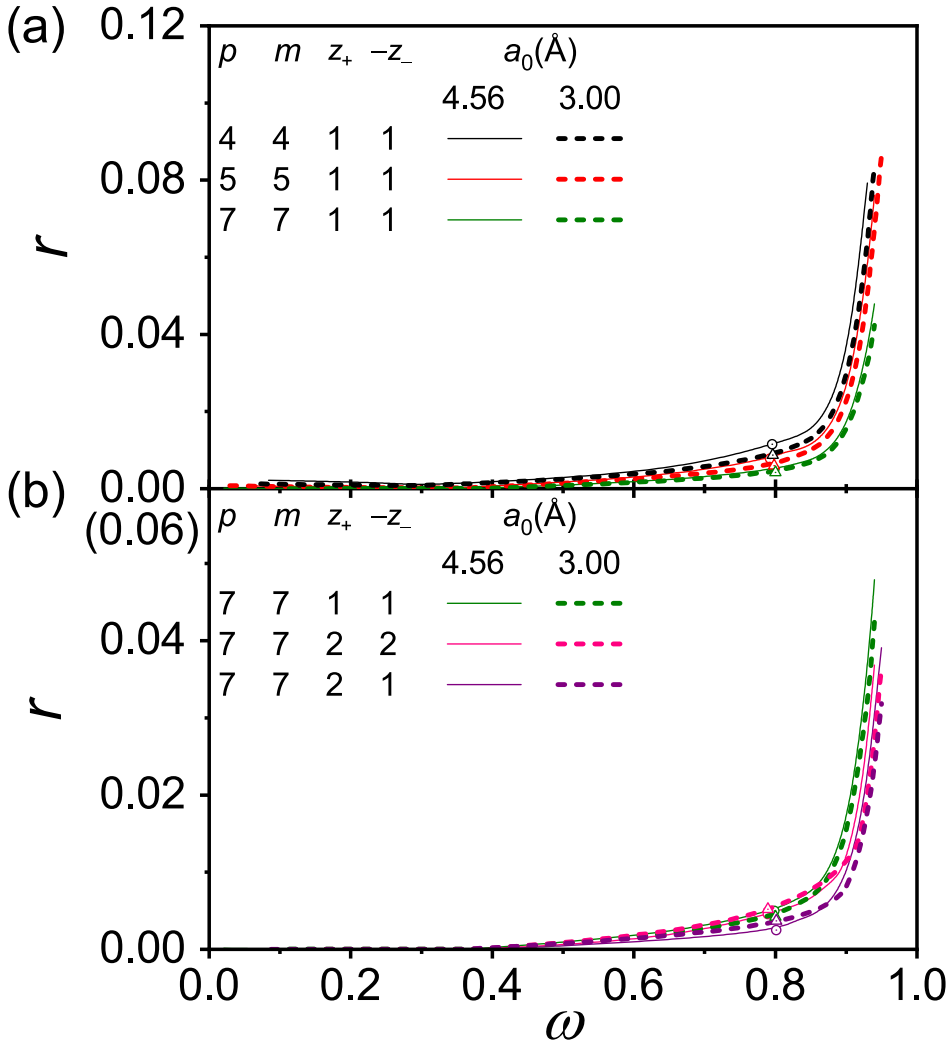

Figure S3: Comparison of theoretical phase diagrams of the WAS system calculated by using Debye radius of 4.56 Å and 3.00 Å. Circles are the critical points for 4.56 Å and triangles for 3.00 Å.

Preferential binding coefficient between acetonitrile and salt

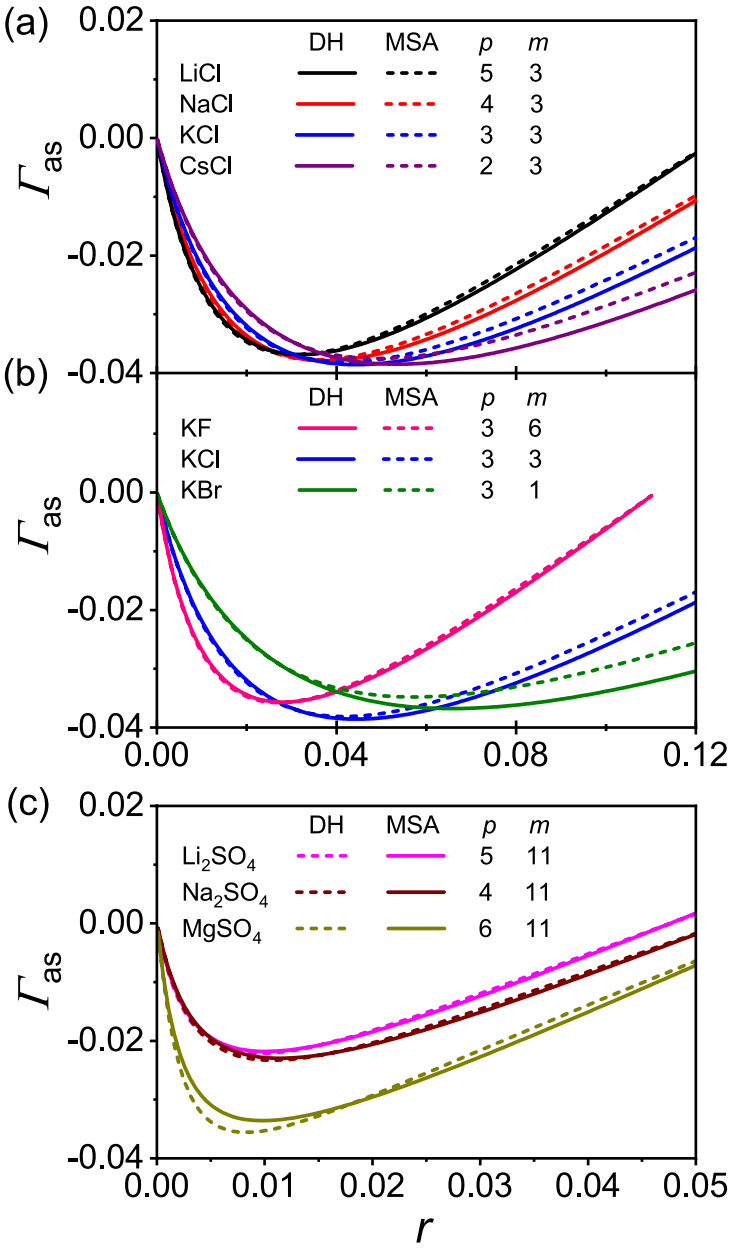

Figure S4: Binding coefficient between acetonitrile and salt $\Gamma_{\rm as}$ as a function of salt concentration r at $\omega = 0.99$.

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